REMARKS

Claims 1-14 stand rejected. Claims 3-4 have been cancelled. Claims 1, 5, 6, 8, 11, 13 and 14 have been amended. Support for the amendments can be found throughout the specification, specifically paragraphs 23-36 and 37-52 inclusive. Claims 1-2 and 5-14 are therefore now pending.

I. Priority:

The Examiner alleges that a certified copy of the priority document EP 02026342.2, filed November 22, 2002, is missing and that the conditions of 35 USC 119 (a-d) have not been met. Applicants note for the record that a certified copy of the priority document (EP 02026342.2, filed November 22, 2002) was supplied to the Patent and Trademark Office on September 1, 2004. Applicants hereby attach a copy of the September 3, 2004 postmarked receipt from the Patent and Trademark Office evidencing said submittal. Applicants herein also attach another copy of the priority document for the Examiner's file. Accordingly, Applicants respectfully submit that the conditions of 35 U.S.C. 119 (a-d) have been met.

II. Claim Rejections

A. 35 USC 112, first paragraph

Claims 1-3 and 5-14 stand rejected by the Examiner under 35 USC 112, first paragraph, for lack of written description. Specifically, the Examiner contends that the claims encompass fragments and alleges that the specification does not show retention of function for the fragments (analogs) to demonstrate possession of the genus as claimed in the invention. Applicants respectfully traverse.

With regard to Claims 1-2 and 5-14, as amended, Applicants respectfully wish to point out that each claim specifically describes and identifies the protein or analogs claimed, with reference to words, structures and formulae that fully set forth the claimed invention (*Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). For example, Claims 1, 5, 6, and 13 specifically recite or depend

upon a reference structure (SEQ ID NO:1) for the claimed protein, with Claim 5 specifically listing the modification sites with reference to the reference structure and Claim 6 listing specific analogs of the protein of Claim 1. In addition, Claims 8-12 specifically set forth the limit of said ranges for each of the component parts of the conjugate of the reference structure and its molecular weight and its activity. Support for these claims are found generally throughout Applicants' specification and specifically with regard to paragraphs 23-36 inclusive, and paragraphs 37-52 inclusive demonstrate and describe how to produce said conjugates as claimed. The Examiner acknowledges that the species are adequately described. As the species have included unpegylated and pegylated erythropoietin conjugates, 1-6 glycosylation sites and erythropoietin conjugates with 1-6 glycosylation sites (as depicted in various formula in the specified paragraphs above, as well as methods for making same) collectively hereinafter referred to as "EPO stimulating agents" or "ESA" of the invention, Applicant respectfully submits that the genus has been sufficiently described and disclosed in drawings/structural formula to show Applicant's possession of the claimed genus and thus also, the claimed invention.

B. 35 USC 112, first paragraph

Claims 1-3 and 5-14 stand rejected by the Examiner under 35 USC 112, first paragraph, for lack of enablement. Specifically, the Examiner contends that the specification, while being enabling for the method of treating disturbances in iron distribution, does not provide enablement for the use of analogs of EPO (protein) in said method. The Examiner contends that the claims encompass an unspecified number of analogs, unlimited free amino groups and no structure of the EPO protein used in the claimed method.

With regard to Claims 1-2 and 6-15, as amended, Applicants respectfully wish to point out that each claim specifically describes and identifies the protein or specific analogs claimed, with reference to words, structures and formulae that fully set forth the claimed invention (*Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41

USPQ2d 1961, 1966 (Fed. Cir. 1997) so that one of ordinary skill in the art could practice the claimed invention. Claims 1, 5, 6, and 13 for example specifically recite or depend upon a reference structure (SEQ ID NO:1) for the claimed protein, with Claim 5 specifically listing the modification sites with reference to the reference structure and Claim 6 listing specific analogs of the protein of Claim 1. In addition, Claims 8-12 specifically set forth the limit of said ranges for each of the component parts of the conjugate of the reference structure and its molecular weight and its activity. Support for these claims are found generally throughout Applicants' specification and specifically with regard to paragraphs 23-36 inclusive, and paragraphs 37-52 inclusive demonstrate and describe how to produce said conjugates as claimed. The Examiner acknowledges that the species are adequately described and enabled. As the described and enabled species have included the "ESA" of the invention (as depicted in various formula in the specified paragraphs above, as well as methods for making same), Applicant respectfully submits that the genus has been sufficiently described and disclosed in drawings/structural formula, as well as depicting a specified amount of analogs, a specified range on the number of amino groups, to enable a skilled artisan to practice the invention as presently claimed. Accordingly, Applicants respectfully submit that the invention as claimed within claims 1-2 and 5-14 is enabled and thus the 112 rejection is overcome.

C. 35 USC 112, second paragraph

Claims 8 and 11 stand rejected for lack of clear antecedent basis for the phrase "the erythropoietin protein is a conjugate" as original claim 1 recites "human erythropoietin". The Examiner alleges no antecedent basis for conjugate or protein in claim 1.

As noted above, Applicants have amended Claims 8 and 11 to reflect "a conjugate of human erythropoietin protein of SEQ ID NO:1", thus providing antecedent support for dependent Claims 9-10 and 12 respectively. As amended claims 8 and 11

are independent claims, said amendment obviates the ground of the rejection for claims 8 and 11.

Accordingly, Applicants respectfully submit that the Section 112 rejections of Claims 8 and 11 is obviated and thus said claims are in condition for allowance.

D. 35 USC 102 (b)

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Silverberg et al. (Journal of the Amer. College of Cardiology, vol. 37, pages 1775-1780, June 1, 2000). This rejection is traversed.

Silverberg et al., is crediting with disclosing a treatment method for anemia (disturbance of iron) in patients with congestive heart failure (CHF) by administering erythropoietin (EPO) and intravenous iron, (see page 1775 of the reference). As the Examiner acknowledges, Silverberg's method necessarily includes IV iron (Abstract background, Abstract methods, Abstract conclusions). Nowhere does Silverberg address treatment with only an EPO alone for this indication.

In Applicants specification the term "disturbances of iron distribution" reflect conditions or states in which the overall concentration of iron in the body is normal, but distributed unequally (large amounts in various organs, small amounts for incorporation into hemoglobin ("lowered concentration of hemoglobin in reticulocytes") and thus akin to anemic effects). See e.g., paragraphs 3-4, 10 of Applicant's specification. Applicants' invention relates to those with heart disease...who have normal amounts of iron but low concentration of hemoglobin (i.e. iron distribution disturbance) and treatment of these individuals with an "ESA", not EPO-α + iron. Claim 1 as amended, specifically recites this. See e.g., paragraphs 5-6, 13 and rest of Applicant's specification.

Applicant's invention specifically warns against exceeding the normal overall concentration of iron in the body (paragraphs 2,3), which could possibly result if one was to follow the teachings of Silverberg et al. Thus, Silverberg fails as a 102(b) anticipatory reference, as it includes and requires an additional element (iron) in its method which is contrary to the teaching and claimed method of Applicant's invention. Accordingly, Applicants respectfully submits that claims 1-2 as amended are now in condition for allowance.

E. 35 USC 103(a)

1. Silverberg in view of Amgen and Hoffmann-La Roche

Claims 1-14 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Silverberg et al. (Journal of the Amer. College of Cardiology, vol. 37, pages 1775-1780, June 1, 2000, (cited on IDS – July 28, 2005)) in view of Amgen (EP 640619, March 1, 1995) and Hoffmann-La Roche (EP 1064 951, January 3, 2001 (cited on IDS – February 13, 2004).

Silverberg et al. is credited with disclosing a treatment method for anemia (disturbance of iron) in patients with congestive heart failure (claim 2) by administering erythropoietin (EPO) and intravenous iron. The Examiner acknowledges that Silverberg et al. does not teach erythropoietin with modifications by adding 1 to 6 glycosylation sites, nor does Silverberg teach ESA (or pegylated erythropoietin conjugates). However, the Examiner contends that both Amgen and Hoffmann-La Roche teaches glycosylation of erythropoietin (see page 2 of the reference); and that Hoffmann-La Roche teach pegylated erythropoietin conjugates and the chemical structures claimed (see claims 7-14, pages 1-5 of the reference), and that it would have been obvious to one of ordinary skill in the art to combine the teachings of the references. The Examiner contends the modification would arise from the alleged teachings of Silverberg (erythropoietin is known in the art to treat anemia (iron disturbance) in patients) and Hoffmann-La Roche (teach erythropoietin for the same purpose and that

As noted above, Silverberg at best teaches and requires EPO plus intravenous iron in its method treatment of CHF. Silverberg therefore requires iron. Even if one skilled in the art was motivated to combine the Hoffmann-La Roche '951 patent and Amgen patent with Silverberg, there is no teaching to delete the required addition of iron in the Silverberg reference. As such, the combination of Silverberg with Amgen and Hoffmann-La Roche do not teach Applicant's invention. Moreover, as Applicant's invention specifically warns against exceeding the normal level of iron concentration in the body, the combination of Silverberg, Amgen and Hoffmann would teach away from Applicants invention as said combination would require concomitant addition of iron to those patients who suffer from CHF. Accordingly, as the cited references do not teach Applicants invention but actually teach away from same, Applicants respectfully submit that claims 1-2, and 5-14 as now presented are in condition for allowance.

2. Silverberg in view of Hoffmann-La Roche

Claims 1-14 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Silverberg et al. (Journal of the Amer. College of Cardiology, vol. 37, pages 1775-1780, June 1, 2000, (cited on IDS – July 28, 2005)) in view of Hoffmann-La Roche (EP 1064 951, January 3, 2001 (cited on IDS – February 13, 2004).

Silverberg et al. is again credited with disclosing a treatment method for anemia (disturbance of iron) in patients with congestive heart failure (claim 2) by administering an EPO and intravenous iron. The Examiner acknowledges that Silverberg et al. does not teach erythropoietin with modifications by adding 1 to 6 glycosylation sites, nor does Silverberg teach any pegylation of erythropoietin or ESA. However, the Examiner contends that Hoffmann-La Roche teaches glycosylation of erythropoietin (see page 2 of the reference); and pegylated erythropoietin conjugates and the chemical structures claimed (see claim 4 and 7-15, pages 1-5 of the reference), and that it would have been obvious to one of ordinary skill in the art to combine the teachings of the references. The Examiner contends the modification would arise from the alleged teachings of

Silverberg (erythropoietin is known in the art to treat anemia (iron disturbance) in patients) and Hoffmann-La Roche (teach pegylated erythropoietin conjugates increased half-life is achieved). Applicants respectfully traverse.

As noted above, Silverberg at best teaches and requires EPO plus intravenous iron in its method treatment of CHF. Silverberg therefore requires iron. Even if one skilled in the art was motivated to combine the Hoffmann-La Roche '951 patent with Silverberg, there is no teaching to delete the required addition of iron in the Silverberg reference. As such the combination of Silverberg and Hoffmann-La Roche do not teach Applicant's invention. Moreover, as Applicant's invention specifically warns against exceeding the normal level of iron concentration in the body, the combination of Silverberg and Hoffmann would teach away from Applicants invention as said combination would require concomitant addition of iron to those patients who suffer from CHF. Accordingly, as the cited references do not teach Applicants invention but actually teach away from same, Applicants respectfully submit that claims 1-2 and 5-14 as now presented are in condition for allowance.

F. The Double Patenting Rejection

1. Claims 1 and 3-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 4-15 of copending application USSN 11/013,560. As said claims of USSN 11/013,560 are not allowed, applicants respectfully submit that this rejection is premature. Applicants request that the double patenting rejection be held in abeyance until there is an indication of allowability of the allegedly overlapping claims in both the instant case and USSN 11/013,560, at which point it can be assessed whether the allowed claims may in fact overlap. Without knowing what subject matter ultimately is allowed in both cases, applicants cannot fairly assess the propriety of the double patenting rejection. Applicants submit that if claims 1, and 5-14 of the instant application as well as certain claims 1 and 4-15 of USSN 11/013,560 are allowed in their current form, Applicants will tender a terminal disclaimer in the latest case that is allowed.

2. Claims 1 and 3-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 3-12 of copending application USSN 10/634,477 (CD 21368). As claims 1 and 3-12 of USSN 10/634,477 are not allowed, Applicants respectfully submit that this rejection is premature. Furthermore, as amended claims 1-2 and 5-14 herein require the absence of iron in the claimed methods, Applicants respectfully submit that these claims are patentably distinct over claims 1, 3-15 and 17-26 of USSN 10/634,477 (which does not require the absence of iron in said claimed methods). Accordingly, Applicants respectfully request the Examiner to withdraw the double patenting rejection.

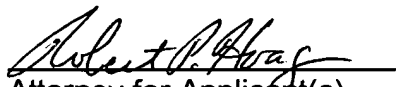
CONCLUSION

The foregoing amendment is fully responsive to the Office Action issued March 13, 2006. Applicants submit that claims 1-2 and 5-14, as amended, are allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,



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